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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicant:	Katsura Funayama et al.
International Publication Number:	WO 2005/056035
International Filing Number:	PCT/JP2004/0018370
International Filing Date:	9 December 2004
Title:	ALGA EXTRACT AND SUGAR HYDROLASE INHIBITOR CONTAINING THE SAME
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February 21, 2007

PROTEST UNDER 37 CFR § 1.291

Attention: Office of Petitions
Commissioner for Patents
P.O. Box 1450
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U.S.A.

Sir :

It is submitted that the present is the first protest submitted in the application by the real party in interest so that 37 CFR 1.291(e) does not apply.

The following presents arguments showing that the claims on file for the subject patent application are not patentable.

The subject claims relate to *Ascophyllum nodosum* extracts, as well as to compositions containing such extracts, for use as inhibitors of glycosidase and in methods of treatment for diabetes.

2. CITABLE PRIOR ART

Barwell *et al.* (1989)

Citable prior art under 35 U.S.C. § 102(b)

Published in 1989, before the filing of the priority claimed for the subject patent application, December 10, 2003.

This reference discloses an extract of *Ascophyllum nodosum* which inhibits α-amylase (see Tables 1, 2 and 3 for instance). The effect on such digestive enzymes suggested potential use of the extract in modulating mammalian digestion (see p. 322, right column, par. 2 for instance). Polyphenols were isolated from the extracts and identified as α-amylase inhibitors (see for instance P. 322, left column, par. 1).

Furthermore, Barwell *et al* teaches that the extracts that it discloses may be used as feed-stuffs for animal or human health foods (see p. 322, right column, par. 2 for instance).

Koukiekolo *et al.*(1999); Chang *et al.* (2004); Precose prescribing information (revised in 2004) and Tormo *et al.* (2006)

Citable prior art under 35 U.S.C. § 102(b)

Published in 1999, before the filing of the priority claimed for the subject patent application, December 10, 2003. Cited references published after this date (i.e., in 2004 to 2006) are provided in support of prior art published before this date.

Koukiekolo *et al.* discloses the capacity of a kidney bean alpha-amylase inhibitor and of acarbose to inhibit porcine pancreatic alpha-amylase *in vitro* (see Tables 2 and 3 for instance).

Chang *et al.* discloses that acarbose treatment of human subjects resulted in significant reductions in fasting and postprandial glucose levels compared with a placebo treatment (see Table 2 for instance).

The Precose prescribing information provides clinical pharmacological information regarding acarbose, as an inhibitor of pancreatic alpha-amylase and intestinal alpha-glucosidase. Acarbose administration is shown to contribute to delayed glucose absorption and a lowering of postprandial hyperglycemia in humans affected by diabetes (see Tables 1 to 3 for instance). Precose was approved for use as a treatment of diabetes in humans by the FDA on September 6, 1995, well before the filing of the priority claimed for the subject patent application, on December 10, 2003.

Tormo *et al.* discloses that a purified pancreatic alpha-amylase inhibitor (alpha-AI) from *Phaseolus vulgaris* administered orally to non-diabetic and type 2 diabetic mice resulted in a reduction in glycemia (see Fig. 1 for instance).

Lamela *et al.* (1989)

Citable prior art under 35 U.S.C. § 102(b)

Published November 1989, before the filing of the priority claimed for the subject patent application, on December 10, 2003.

This reference discloses the therapeutic value of preparations extracted from several species of algae, as treatments against diabetes (see p. 35, Introduction, lines 1-10).

Hence this reference discloses algal extracts from *Laminaria ochroleuca*, *Saccorhiza polyschides* and *Fucus vesiculosus*. Oral administration of *F. vesiculosus* extracts caused a significant reduction in blood glucose in normal rabbits (see p. 39, lines 12-18 and p. 38, Table 1 for instance).

This reference further discloses polysaccharide extracts from algal species *Himanthalia elongata* and *Codium tomentosum*. Intravenous administration of *H. elongata* polysaccharide extracts caused a significant reduction (about 18%) in the glycemia of normal rabbits (see. p. 39, lines 30-35, and p. 41, Table 3 for instance). Furthermore, intravenous administration of such polysaccharide extracts also caused a significant reduction (about 50%) in the glycemia of alloxan-treated (chronically hyperglycemic or diabetic) rabbits (see p.42, lines 1-7, and Figure 1 for instance).

Hosoyama *et al.* (2003)

Citable prior art under 35 U.S.C. § 102(a)

Published online on May 1 2003 before the filing of the priority claimed for the subject patent application, on December 10, 2003.

This reference discloses that extracts from Banaba (*Lagerstroemia speciosa*) leaf inhibit alpha-amylase activity *in vitro* (see Fig. 3 and 4 for instance), suggesting that this effect was at least partly responsible for use of Banaba as a folk medicine against diabetes.

Ohta *et al.* (2002) and Han *et al.* (2003)

Citable prior art under 35 U.S.C. § 102(a)

Published in 2002 and on December 5, 2003, respectively, before the filing of the priority claimed for the subject patent application, on December 10, 2003.

These references disclose phenolic extracts from dietary plant and algal sources having anti alpha-amylase activity and anti-glucosidase, sucrase and maltase activities *in vitro*.

These references also disclose that these extracts have anti-diabetic and anti-obesity effects *in vivo*.

3. ARGUMENT

A. NOVELTY

It is submitted that Barwell *et al.* anticipates claims 1 to 3, 5 and 7, in that it explicitly discloses an *Ascophyllum nodosum* extract and purified fractions thereof which inhibits, alpha-amylase amongst other digestive enzymes (see Tables 1-3 for instance). Barwell *et al* also teaches that the extracts that it discloses may be used as feed-stuffs for animal or human health foods (see p. 322, right column, par. 2). From the specification of the subject application, it is understood that that the claimed term "glycosidase" is meant to refer to alpha-amylase, maltase and sucrase for instance (see page 15, Table 2 of the subject application for instance).

B. INVENTIVE STEP

Methods of Treatment of Diabetes

It is submitted that a person of ordinary skill in the art would have been led to combine the teachings of Barwell *et al.* with those the other above-cited references to achieve the claimed methods of treatment of diabetes. Barwell *et al.* teaches that *Ascophyllum nodosum* extracts displayed significant inhibitory activity towards glycosidase and other digestive enzymes, with potential applications in treating diabetes.

Several references confirm that extracts from a variety of dietary plant and algal sources displaying inhibitory activity *in vitro* against glycosidase, possess *in vivo* effect against diabetes and the ability to reduce diabetes associated symptoms (e.g. obesity, elevated blood glucose).

Ohta *et al.* (2002) disclose an extract from the brown algae Ezoishige (*Pelvetia babingtonii*) with the capacity to inhibit rat-intestinal sucrase and maltase activities *in vitro* (see Fig. 1 for instance). Furthermore, Ohta *et al.* disclose a 70% polysaccharide-containing extract with the capacity to suppress the postprandial elevation in blood glucose after its oral administration to rats (see Fig. 2 for instance), suggesting a potential role for extracts from brown algae as dietary treatments against elevated blood glucose, diabetes and obesity (see p.1554, left column, lines 10-14).

Hosoyama *et al.* (2003) disclose that extracts from Banaba (*Lagerstroemia speciosa*) leaf inhibit alpha-amylase activity *in vitro* (see Fig. 3 and 4 for instance), suggesting that this effect was at least partly responsible for use of Banaba as a folk medicine against diabetes.

Lamela *et al.* teaches that administration of polysaccharide-containing extracts from various species of algae can significantly reduce blood glucose levels in normal and diabetic rabbits (see p. 39, lines 30-35, p. 41, Table 3, and p.42, lines 1-7, and Figure 1).

The references Koukiekolo *et al.*(1999); Chang *et al.* (2004) (see whole reference and in particular lines 18-28 of the abstract for instance); Precose prescribing information (revised in 2004) (see whole reference and in particular lines 1 and 2 of page 1) and Tormo *et al.*

(2006) (see whole reference and in particular abstract for instance), together, provide *in vitro* and *in vivo* evidence for the capacity of the alpha-amylase inhibitor acarbose and kidney bean alpha-amylase inhibitor to reduce glucose absorption and elevated blood glucose, in the treatment of diabetes in humans.

Han *et al.* (2003) disclose polyphenol fractions extracted from the leaves of *Salix matsudana* that inhibit alpha-amylase activity *in vitro* (see Table 5) and that provide several anti-obesity effects following oral administration to mice fed a high-fat diet (see p. 1193, left column, lines 23-34 and p. 1193, right column, lines 34-42 for instance), including inhibiting the absorption of ingested dietary fat (see Table 2 for instance), suppressing body weight gain (see Fig. 2 for instance) at 2-9 weeks, suppressing final parametrial adipose tissue weight gain (see Fig. 3a for instance), suppressing the increase in adipocyte diameter (see Fig. 3b for instance) and enhancing norepinephrine-induced lipolysis in adipocytes *in vitro* (see Table 4 for instance).

From these teachings, a person skilled in the art would expect that *Ascophyllum nodosum* extracts, which are known to have inhibitory activity against alpha-amylase, will have therapeutic value against diabetes in mammals. Accordingly, these teachings render claims 4, 6 and 8 obvious.

Notification has been served on the applicant's Attorney, Iwatani Patent Office, on February 19, 2007 by FedEx, Tracking Number 8590 1433 0940. For your convenience, a copy of the Way Bill is attached.

Authorization is hereby given to charge Deposit Account no. 07-1742 for any deficiencies or overages in connection with this response.

Respectfully submitted,

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